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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,137	08/01/2001	George Heavner	CEN0250	5801

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,137	HEAVNER ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2004 and 11 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action in response to Applicants response filed 5/7/2004 and the sequences compliance of 4/11/2005. Claims 1, 9 and 16 are amended. Claims 1-3, 9 and 16 are pending.

2. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

3. The Office acknowledges the receipt of the drawings on 5/6/2002.

Specification

4. Although, Applicants have changed the title of the invention, the disclosure is objected to because of the following informalities: The blanks present throughout the specification (see pages 28 and 98). In addition, the tables present on pages 39, 94, 101, 110 and 111 lack the table numbers. Appropriate correction is required.

5. All the pending rejections are withdrawn because they were made assuming SEQ ID NO: 7 and 8 described MIP-1b and RANTES sequences respectively.

Claim Rejections - 35 USC § 112

6. Claims 1-3, 9 and 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claims 1-3, 9 and 16 are rejected as vague and indefinite because Applicant's recitation of "at least one". It is unclear if Applicant intends to claim a composition comprising at least one antibody. The Office does not know how many antibodies are claimed how they might differ from each other.

6b. Claim 3 is rejected as vague and indefinite for claiming, "neutralizes at least one activity of at least one TNF protein". It is unclear which activity of the TNF protein will be neutralized by the instant invention.

7a. Claims 1, 9 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for human anti TNF antibody comprising a heavy or light variable region Of SEQ ID NO: 7 and 8, does not reasonably provide enablement for all mammalian anti TNF antibodiescomprising at least SEQ ID NO: 7 and SEQ ID NO: 8 as a variable region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 1, 9 and 16 are drawn to mammalian anti-TNF antibody having at least one variable region comprising SEQ ID Nos: 7 and 8. The specification defines SEQ ID Nos: 7 and 8 as human variable regions. The specification also states that the anti-TNF antibody comprises at least of heavy chain variable region, optionally having the amino acid sequence of SEQ ID NO: 7 and/or at least one light chain variable region, optionally having the amino acid sequence of SEQ ID NO: 8 (see paragraph 105, lines 16-20). The SEQ ID NO: 7 and SEQ ID NO: 8 are both human polypeptide sequences. Virtually all polypeptides are immunogenic when exposed to various organisms' immune systems. Although the specification describes human anti-TNF antibodies comprising SEQ ID NO:7 and SEQ ID NO: 8, the specification does not teach how to generate various mammalian anti-TNF antibodies comprising SEQ ID NO: 7 and SEQ ID NO: 8 as contemplated by the instant invention. In the instant application, there is insufficient guidance regarding how to make the genus of mammalian anti-TNF antibodies with SEQ ID NO: 7 and SEQ ID NO: 8 as variable regions. There are no examples of other mammalian anti-TNF antibodies that comprise SEQ ID NO: 7 and SEQ ID NO: 8 The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to generate the antibodies. Although the specification outlines art-recognized procedures for producing antibodies, this is not adequate guidance as to the nature of active derivatives that may be

constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

A large quantity of experimentation would have been necessary for the skilled artisan to generate all mammalian anti-TNF antibodies with human SEQ ID NO: 7 and SEQ ID NO: 8 as variable regions recited in the claims and possibly screen the same for a useful activity. The specification fails to provide sufficient direction/guidance regarding which structural features are required in order to provide mammalian anti-TNF antibodies with SEQ ID NO: 7 and SEQ ID NO: 8 as variable regions for a specific activity. There are no working examples directed to mammalian anti-TNF antibodies with SEQ ID NO: 7 and SEQ ID NO: 8 as variable regions. The nature of the invention is complex, involving the generation of mammalian anti-TNF antibodies with human SEQ ID NO: 7 and SEQ ID NO: 8 as variable regions and screening them for a useful activity. The state of the prior art establishes the unpredictability of the effects of antibodies. Finally, the breadth of the claims is large, failing to recite any structural or functional limitations. For all of these reasons, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

7b. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the administration or contacting human anti TNF antibody by intraperitoneal administration, does not reasonably provide enablement for the administration or contacting human anti TNF antibody by parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular,

intracartilaginous, intracavitary, intracelial, intracelebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses only the intraperitoneal administration of human anti-TNF antibody in mice (see examples 4-7). A large quantity of experimentation would have been necessary for the skilled artisan to administer the anti-TNF antibody by the various methods described because the specification fails to provide sufficient direction/guidance regarding the various methods. In addition, it is also unclear what specific activity is being neutralized in the instant invention. There are no working examples disclosing the various methods of the administration of the anti-TNF antibodies. The nature of the invention is complex, involving the administration to various target tissues using the claimed methods. The state of the prior art establishes the unpredictability of the effects of antibodies. Finally, the breadth of the claims is large, failing to recite any specific activity or targeted tissue. For all of these reasons, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

8. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSS 06/05

JANET ANDRES
PRIMARY EXAMINER